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STRUCTURAL AND MORPHOMETRIC REMODELING OF THE SPLEEN IN EXPERIMENTAL CHRONIC KIDNEY DISEASE

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Abstract

The spleen, as a major secondary lymphoid organ involved in systemic immune surveillance, antigen presentation, lymphocyte maturation, and hematological filtration, may therefore represent an important morphological target of chronic renal dysfunction. The present study aimed to characterize the morphological and morphometric remodeling of the spleen under conditions of experimentally induced chronic kidney failure and to determine the structural parameters that most adequately reflect systemic renal-associated immune and hematological disturbances. Experimental animals were divided into control and chronic kidney disease groups. Histological examination of splenic tissue was performed with assessment of the capsule, trabecular framework, white pulp, red pulp, lymphoid follicles, periarteriolar lymphoid sheaths, marginal zones, and vascular components. Quantitative morphometric analysis included determination of the relative areas of white and red pulp, number and diameter of lymphoid follicles, vascular parameters, and stromal components.

Keywords: chronic kidney disease, chronic renal failure, spleen, morphometry, histomorphometry, white pulp, red pulp, lymphoid follicles, immune dysfunction, uremia.



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Relevance

Chronic kidney disease is increasingly recognized as a systemic disorder rather than an isolated renal pathology. Progressive reduction in glomerular filtration is accompanied by the accumulation of uremic solutes, disruption of endocrine and metabolic functions, anemia, oxidative imbalance, endothelial dysfunction, and persistent activation of inflammatory pathways[1]. These processes contribute substantially to the development of extra-renal complications and influence the structural organization of multiple organs. Among the systems affected by chronic renal dysfunction, the immune system occupies a particularly important position. CKD is characterized by a complex state of simultaneous immune activation and immune incompetence. Chronic exposure to uremic toxins and inflammatory mediators may promote persistent innate immune activation while impairing adaptive immune responses[2]. Consequently, patients with advanced renal dysfunction demonstrate increased susceptibility to infectious complications, altered inflammatory responses, and impaired immunological surveillance. The spleen is a highly organized lymphoid organ that integrates immune and hematological functions. Its white pulp contains lymphoid compartments responsible for adaptive immune responses, whereas the red pulp is predominantly involved in blood filtration, erythrocyte clearance, and vascular regulation[3]. Because these functional compartments have distinct cellular and microvascular organization, their quantitative relationship may provide valuable morphological information concerning systemic pathological processes. Therefore, quantitative assessment of splenic microarchitecture may provide additional insight into the mechanisms linking renal failure with systemic immune and hematological disturbances.



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Purpose of the study

To study the comparative characteristics of morphological and morphometric parameters of the spleen in chronic renal failure.

Materials and methods of research

An experimental model of chronic kidney dysfunction was established in laboratory animals. At the beginning of the experiment, all sexually mature rats were quarantined for one week, and after excluding somatic or infectious diseases, they were transferred to the usual vivarium regimen with three meals a day. During the experiment, taking into account the generally accepted timing of renal failure development, observations were conducted at 3 days, 1 and 2 weeks, as well as after 1 month. Histomorphological assessment included evaluation of the general splenic architecture, fibrous capsule, trabecular system, white and red pulp, lymphoid follicles, periarteriolar lymphoid sheaths, marginal zones, splenic sinusoids, and vascular structures. Morphometric analysis was performed using quantitative assessment of the relative area of white pulp and red pulp, lymphoid follicle number and mean diameter, vascular dimensions, and stromal components. The white-to-red pulp ratio was considered an integrated parameter reflecting the structural balance between immunological and hematological compartments of the spleen.

Research results

Experimental chronic kidney dysfunction was associated with pronounced remodeling of the splenic microarchitecture. The most informative changes involved the lymphoid component of the white pulp, the relative representation of the red pulp, and the structural organization of vascular and stromal elements. The white pulp demonstrated quantitative and architectural alterations of



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lymphoid follicles and periarteriolar lymphoid compartments. Such changes may be interpreted in the context of the complex immunological response associated with chronic uremia. During the initial stages of systemic renal dysfunction, persistent antigenic stimulation and inflammatory activation may result in compensatory lymphoid responses. However, prolonged exposure to uremic toxins and oxidative stress may subsequently impair lymphocyte proliferation, differentiation, and functional competence, leading to structural regression of lymphoid compartments.

A reduction in the relative white pulp area and alterations in follicular dimensions may therefore represent morphological manifestations of impaired adaptive immune organization. Importantly, these changes should not be interpreted as isolated local abnormalities. Rather, they may reflect the systemic consequences of chronic renal dysfunction on immune homeostasis. The red pulp demonstrated a different pattern of structural remodeling. CKD-associated anemia, altered erythrocyte turnover, changes in blood rheology, and disturbances of splenic filtration may increase the functional burden placed on the red pulp. Consequently, changes in sinusoidal architecture, vascular filling, and stromal organization may develop.

Of particular interest is the alteration of the white-to-red pulp ratio. This parameter may serve as an integrated morphometric indicator of the balance between the immunological and hematological functions of the spleen. A relative reduction in white pulp accompanied by expansion or predominance of red pulp may indicate a shift from an immunologically active lymphoid architecture toward a pattern associated with enhanced hematological and filtration demands. The observed remodeling may be mediated through several interconnected mechanisms. Uremic retention solutes can alter leukocyte function and endothelial signaling, while oxidative stress promotes cellular injury and



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extracellular matrix remodeling. From a methodological perspective, quantitative histomorphometry provides an important advantage over purely descriptive morphological assessment. Measurements of white pulp area, follicular dimensions, follicular density, vascular parameters, and white-to-red pulp ratio allow subtle structural changes to be detected and objectively compared between experimental groups. Furthermore, age-related changes in splenic architecture should be considered when interpreting experimental results. The incorporation of age-matched control groups and standardized morphometric criteria is therefore essential for distinguishing physiological remodeling from pathological alterations induced by chronic renal dysfunction.

Conclusion

Experimental chronic kidney disease induces substantial morphological and morphometric remodeling of the spleen, involving both immunological and hematological compartments. Alterations in white pulp organization, lymphoid follicular architecture, red pulp representation, and vascular-stromal components indicate that chronic renal dysfunction exerts a systemic effect on splenic microarchitecture. The white-to-red pulp ratio, together with quantitative characteristics of lymphoid follicles and vascular structures, may represent valuable morphometric indicators of CKD-associated systemic remodeling. These structural alterations are likely to reflect the combined effects of uremic toxicity, chronic inflammation, oxidative stress, anemia, and immune dysregulation. Comprehensive histomorphometric evaluation of the spleen may therefore contribute to a better understanding of the extra-renal manifestations of chronic kidney disease and provide a morphological basis for investigating the kidney-immune system-spleen axis in progressive renal dysfunction.



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